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EXAMINER
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STRZELECKA, TERESA E

ART UNIT	PAPER NUMBER
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1637

NOTIFICATION DATE	DELIVERY MODE
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05/06/2008

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/516,982	<b>Applicant(s)</b> KADONAGA ET AL.	
	<b>Examiner</b> TERESA E. STRZELECKA	<b>Art Unit</b> 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 January 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1 and 4-33 is/are pending in the application.
- 4a) Of the above claim(s) 4,6,7,9,11,12,14,15,18,20 and 22-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,5,8,10,13,16,17,19,21 and 30-33 is/are rejected.
- 7) ☒ Claim(s) 1,5,8,10,13,16,17,19,21 and 32 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. This office action is in response to an amendment filed January 14, 2008. Claims 1-30 were previously pending, with claims 4, 6, 7, 9, 11, 12, 14, 15, 18, 20 and 22-29 withdrawn from consideration. Applicants cancelled claims 2 and 3, and amended claims 1, 5, 10, 13, 19, 21 and 30, and added new claims 31-33 (Applicants indicated claim 31 as “previously presented”, however, it is a new claim). Claims 1, 5, 8, 10, 13, 16, 17, 19, 21 and 30-33 will be examined.

2. Applicants’ submission of a new sequence listing obviated the objections presented in the previous office action.

3. Applicants’ amendments overcame the rejection of claims 1-3, 13, 16 and 30 under 35 U.S.C. 101; rejection of claims 5 and 10 under 35 U.S.C. 112, second paragraph; and the rejection of claims 1-3, 16 and 30 under 35 U.S.C. 102(b) as anticipated by Kanaar et al.; rejection of claims 2 and 3 under 35 U.S.C. 102(b) as anticipated by Wiesmuller et al. and rejection of claims 2 and 3 under 35 U.S.C. 102(b) as anticipated by Datta et al. All other previously presented rejections are maintained for reasons given in the “Response to Arguments” section below.

### ***Response to Arguments***

4. Applicant's arguments filed January 14, 2008 have been fully considered but they are not persuasive.

A) Regarding the rejection of claims 1, 10, 13, 16, 17, 19, 21 and 30 under 35 U.S.C. 102(b) as anticipated by Wiesmuller et al., Applicants argue that Wiesmuller et al. do not teach contacting an isolated polynucleotide with proteins to form a nucleosomal polynucleotide comprising histones.

However, Wiesmuller et al. teach introduction of isolated SV40 DNA into monkey cells, where the DNA becomes associated with histones, as evidenced also by Polisky et al., therefore the reference inherently teaches this limitation. Further, Wiesmuller et al. specifically teach the

following (page 742, second paragraph): "...viral DNA enters and leaves the cell in a chromatin-bound form".

The rejection is maintained.

B) Regarding the rejection of claims 1, 5, 8, 10, 13, 16, 17 and 30 under 35 U.S.C. 102(b) as anticipated by Datta et al., Applicants argue that Datta et al. do not teach or suggest contacting an isolated polynucleotide with proteins to form a nucleosomal polynucleotide comprising histones. However, as explained in the rejection presented in the previous office action, isolated SV40 DNA inherently associates with histones in cells, therefore by teaching contacting isolated polynucleotide with SV40 sequences with a eukaryotic cell extract Datta et al. inherently teach chromatin formation on the DNA.

The rejection is maintained.

### ***Claim Objections***

5. Claims 1, 5, 8, 10, 13, 16, 17, 19, 21, 31 and 32 are objected to because of the following informalities: claim 1 contains a typographical error in line 4: "proteins the promote" should be "proteins that promote". Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The newly added limitation of claim 5 “recombinant recombinase” is not supported by the specification or original claims, therefore it represents new matter.

***Claim Interpretation***

8. Both claims 1 and 30 are interpreted as encompassing in vitro and in vivo homologous recombination processes.

9. Applicants described the term “nucleosomal polynucleotide” on page 8, paragraph [0025], as follows:

“As used herein, a "nucleosomal polynucleotide" includes any nucleic acid associated with histone core proteins, or histone-like core proteins, forming a chromatin-like structure.” Therefore, it is interpreted as any nucleic acid associated with histones or other proteins, as Applicants did not define the terms “histone-like core-proteins” or “chromatin-like structure”.

10. Applicants defined the term “exogenous nucleosomal polynucleotide” on page 10, [0030], as follows:

“As used herein, an "exogenous nucleosomal polynucleotide" is a polynucleotide which is transferred into a target cell but which has not been replicated in that host cell;”

11. Applicants defined the term “target nucleic acid sequence” on page 10, [0032], as follows:

“As used herein, the term "target nucleic acid sequence" refers to polynucleotide sequences suitable for recombination with a nucleosomal polynucleotide.” Therefore the term is interpreted as any nucleic acid sequence.

12. Applicants defined the term “recombinase” on page 11, [0033], as follows:

“As used herein, "recombinase" refers to polypeptides having essentially all or most of the same functions, particularly the recombinase can: (i) properly bind to and position a nucleosomal polynucleotide to a homologous target and (ii) facilitate homologous recombination.”

13. Applicants did not define the term “isolated recombinase”, therefore any recombinase that is not contained within live cells is considered to anticipate this term.

14. Applicants did not define the term “Rad51 associated activity”, therefore it is interpreted as any recombinase activity.

15. Applicants did not define the term “plasmid”, therefore it is interpreted as any nucleic acid vector or virus.

***Claim Rejections - 35 USC § 102***

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 1, 10, 13, 16, 17, 19, 21 and 30-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Wiesmuller et al. (J. Virology, vol. 70, pp. 737-744, 1996; cited in the previous office action), as evidenced by Polisky et al. (PNAS USA, vol. 72, pp. 2895-2899, 1975; cited in the previous office action) and Kanaar et al. (Trends in Cell Biol., vol. 8, pp. 483-489, 1998; cited in the IDS and in the previous office action).

Claims 1 and 30 will be considered together in claim 1, since it is a species of claim 30.

Regarding claims 1 and 30, Wiesmuller et al. teach a method of promoting homologous recombination, the method comprising:

contacting an isolated polynucleotide comprising a desired sequence to be recombined with proteins that promote chromatin formation to generate a nucleosomal polynucleotide comprising histones; contacting, under conditions that support homologous recombination, the polynucleotide with a target nucleic acid, wherein the target nucleic acid comprises a nucleotide sequence

homologous to the nucleosomal polynucleotide; and contacting the nucleosomal polynucleotide and target nucleic acid with a recombinase comprising Rad51 associated activity (Wiesmuller et al. teach providing two SV40-based vectors (=isolated polynucleotides) to study frequency of homologous recombination in monkey PRK cells (page 738, paragraphs 2-4, 10 and 11; page 739, paragraphs 1-3). Wiesmuller et al. teach that SV40 particles form minichromosomes within eukaryotic cells (page 737, last paragraph), as evidenced also by Polisky et al., who teach association of SV40 with histones (page 2895, paragraphs 2-4). Therefore, by teaching SV40 viral particles within eukaryotic cells Wiesmuller et al. teach nucleosomal polynucleotide and target polynucleotide associated with histones. Wiesmuller et al. teach monkey cells (page 738, second paragraph; page 739, third paragraph). Therefore, since mammalian cells perform homologous recombination, Wiesmuller et al. inherently teach Rad51 associated activity. Further, as evidenced by Kanaar et al., mammalian cells contain the Rad51 recombinase (p. 486, Table 1), therefore Wiesmuller et al. inherently teach Rad51.)

Regarding claim 10, Wiesmuller et al. teach transfecting the cells with SV40 viruses, therefore they teach exogeneously prepared target sequences (page 738, last paragraph; page 739, first paragraph).

Regarding claim 13, Wiesmuller et al. teach the target nucleic acid being a coding sequence (page 739, second paragraph).

Regarding claims 16, 32 and 33, Wiesmuller et al. teach association of SV40 into minichromosomes within eukaryotic cells (page 737, last paragraph), as evidenced also by Polisky et al., who teach association of SV40 with histones in monkey cells (page 2895, paragraphs 2-4) and core histones (Abstract; page 2896, paragraphs 4-6). Therefore, by teaching SV40 viral particles

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within eukaryotic cells Wiesmuller et al. teach nucleosomal polynucleotide and target polynucleotide associated with core histones.

Regarding claim 17, Wiesmuller et al. teach SV40 viruses (page 738, third and fourth paragraphs), therefore they teach plasmids.

Regarding claims 19, 21 and 31, Wiesmuller et al. teach one of the SV40 particles comprising sequence which generates a mutation in a target sequence altering its expression and the mutation being point mutation (page 739, second paragraph; Fig. 1).

18. Claims 1, 5, 8, 10, 13, 16, 17 and 30-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Datta et al. (J. Biol. Chem., vol. 276, pp. 18018-18023, May 2001; cited in the previous office action) as evidenced by Polisky et al. (PNAS USA, vol. 72, pp. 2895-2899, 1975; cited in the previous office action).

Claims 1 and 30 will be considered together in claim 1, since it is a species of claim 30.

Regarding claims 1 and 30, Datta et al. teach a method of promoting homologous recombination, the method comprising:

contacting an isolated polynucleotide comprising a desired sequence to be recombined with proteins that promote chromatin formation to generate a nucleosomal polynucleotide comprising histones; contacting, under conditions that support homologous recombination, the polynucleotide with a target nucleic acid, wherein the target nucleic acid comprises a nucleotide sequence homologous to the nucleosomal polynucleotide; and contacting the nucleosomal polynucleotide and target nucleic acid with a recombinase comprising Rad51 associated activity (Datta et al. teach providing an SV40-based plasmid pSupFG1/G144C (= isolated polynucleotide) with a 40 bp fragment homologous to bp 121-160 of the supFG1-144 gene (page 18019, second and third paragraph; Fig. 1) and a donor oligonucleotide (= target nucleic acid) (page 18019, second and



fourth paragraph; Fig. 1) under conditions which promote homologous recombination (page 18019, paragraphs 8 and 9; page 18020, second and third paragraph). As evidenced by Polisky et al. SV40 particles associate with histones (page 2895, paragraphs 2-4), therefore, by teaching SV40 plasmid in eukaryotic cell extract, Datta et al. inherently teach nucleosomal polynucleotides. Datta et al. teach Rad51 associated recombinase activity (page 18019, second paragraph; page 18020, 6<sup>th</sup> paragraph).).

Regarding claim 5, Datta et al. teach recombinase in a cell extract (page 18019, paragraphs 8 and 9), therefore they teach isolated recombinase.

Regarding claim 8, Datta et al. teach recombination in a cell extract in vitro (page 18019, paragraphs 8 and 9).

Regarding claim 10, Datta et al. teach exogenous target sequence (page 18019, fourth paragraph; Fig. 1).

Regarding claim 13, Datta et al. teach a sequence coding for a supFG1-144 gene (Fig. 1).

Regarding claims 16, 32 and 33, Datta et al. teach SV40-based plasmid within eukaryotic cell extract (page 18019, 9th paragraph). As evidenced also by Polisky et al. SV40 particles associate with histones in monkey cells (page 2895, paragraphs 2-4) and core histones (Abstract; page 2896, paragraphs 4-6). Therefore, by teaching SV40 plasmid within eukaryotic cells Datta et al. teach nucleosomal polynucleotide associated with core histones.

Regarding claim 17, Datta et al. teach SV40-based plasmid (Fig. 1).

19. No claims are allowed.

### ***Conclusion***

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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April 29, 2008